

**CLAIMS**

I/We hereby claim:

1. A method of determining a biological age of a human subject, or a rate of biological aging of a human subject, which comprises

(A) assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1A,

and inversely correlating the level of expression of said marker gene with a biological age or a rate of biological aging of said patient, or

(B) assaying tissue or body fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B, and directly correlating the level of expression of said marker gene with a biological age or a rate of biological aging of said subject.

2. The method of claim 1 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

3. The method of claim 1 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.



4. A method of (I) reducing a rate of biological aging in a human subject, and/or (II) delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or (III) protecting against an age-related (senescent) disease, which comprises

administering to the subject a protective amount of an agent which is

(A) (1) a polypeptide which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1A,

or

(2) an expression vector encoding the polypeptide of (A) (1) above and expressible in a human cell, under conditions conducive to expression of the polypeptide of (A) (1); or

(B) (1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B,

(2) an anti-sense vector which inhibits expression of said polypeptide of (B) (1) in said subject,

where said agent reduces a rate of biological aging in said subject, and/or delays the time of onset, or reduces the severity, of an undesirable age-related phenotype in said subject, and/or protects against an age-related disease.

5. The method of claim 4 in which (I) applies.

6. The method of claim 4 in which (II) applies.



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7. The method of claim 4 in which (III) applies.

8. The method of claim 5 in which biological age is measured by a biomarker.

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9. The method of claim 8 in which the marker is a simple biomarker.

10. The method of claim 8 in which the marker is a composite biomarker.

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11. The method of claim 5 in which the affected biological age is the overall biological age of the subject.

12. The method of claim 5 in which the affected biological age is the biological age of a body system of the subject.

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13. The method of claim 5 in which the affected biological age is the biological age of an organ of the subject.

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14. The method of claim 13 in which the organ is the liver.

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15. The method of claim 8 in which at least one marker is the level of a biochemical in the blood of the subject.

16. The method of claim 15 in which the biochemical is growth hormone or IGF-1.

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17. The method of any one of claims 1-16 in which the reference protein is a human protein.

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18. The method of any one of claims 1-16 in which the reference protein is a mouse protein.



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19. The method of claims 1-18 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

5 20. The method of any one of claims 1-18 in which said polypeptide is at least 90% identical to said reference protein.

10 21. The method of claim 20 in which said polypeptide is identical to said reference protein.

15 22. The method of any one of claims 1-21 in which the E-value cited for the reference protein in Master Table 1 is not more than  $e^{-6}$ .

23. The method of claim 22 in which the E-value cited for the reference protein in Master Table 1 is less than  $e^{-10}$ .

20 24. The method of claim 23 in which the E value calculated by BLASTN or BLASTX is less than  $e^{-15}$ , more preferably less than  $e^{-20}$ , still more preferably less than  $e^{-40}$ , further more preferably less than  $e^{-50}$ , even more preferably less than  $e^{-60}$ , considerably more preferably less than  $e^{-80}$ , and most preferably less than  $e^{-100}$ .

25 25. The method of claims 1-24 in which (A) applies.

26. The method of claims 1-24 in which (B) applies.

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27. The method of claim 26 in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.

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28. The method of claim 26 in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.



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29. The method of claim 26 in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.

5           30. The method of claim 29 in which said organic molecule is identifiable as a molecule which binds said polypeptide by screening a combinatorial library.

10           31. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as corresponding to clone 4-11.

15           32. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as corresponding to clone 4-29.

20           33. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as corresponding to clone 4-97.

          34. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as corresponding to clone 4-130.

25           35. The method of any one of claims 1-24, 26-30 in which the reference protein is listed in master table 1 as corresponding to clone 5-105.

30           36. The method of any one of claims 1-24, 26-30 in which the reference protein is listed in master table 1 as corresponding to clone 5-38.

35           37. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as corresponding to clone 5-41.

          38. The method of any one of claims 1-25 in which the reference protein is listed in master table 1 as



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corresponding to clone 5-43.

5       39. The method of any one of claims 1-25 in which the  
reference protein is listed in master table 1 as  
corresponding to clone 5-61.

10       40. The method of any one of claims 1-25 in which the  
reference protein is listed in master table 1 as  
corresponding to clone 5-9.

15       41. The method of any one of claims 1-24, 26-30 in  
which the reference protein is listed in master table 1 as  
corresponding to clone 5-138.